IN THE SPECIFICATION

Please insert the following section on line 4 of the first page of the application following the title of the invention and preceding the section titled, "**BACKGROUND**":

CROSS REFERENCE

This application is a § 371 application of international application number PCT/US2005/004409 filed on 14 February 2005, which claims priority from U.S. provisional application numbers 60/543,880 filed on 12 February 2004 and 60/551,558 filed on 9 March 2004, herein incorporated by reference.

Please replace the paragraph that begins on page 1, line 27 as follows:

An alternative method for generating siRNA relies on *in vitro* transcription (see for example, Donze and Picard, ~~*Nucleic Acids Res.* 30:1757-1766 (2002)~~ *Nucleic Acids Res* 30:e46 (2002) and Paddison et al. *Genes and Dev.* 16:948-958 (2002)). While this approach does not require chemical synthesis, it remains necessary to choose and test individual short sequences to determine which are most effective. In previous studies, the standard siRNA concentration used was above 20nM even as high as 200 nM (Kawasaki et al., *Nucleic Acids Res 31:*981-987 (2003); Elbashir et al., *Nature 411:*494-498 (2001); Wu et al. *Cancer Res.* 63:1515–1519 (2003)). If the concentration is too high, it can provoke non-specific responses (Semizarov et al. *Proc. Natl. Acad. Sci.* 100:6347–6352 (2003); Jackson et al. *Nat. Biotechnol.* 21:635–637 (2003); Persengiev et al. *RNA* 10:15-18 (2003)).

Please replace the paragraph that begins on page 2, line10 as follows:

Several enzymatic approaches have been reported for cleaving double-stranded RNA (dsRNA) molecules into short fragments. An evolutionarily conserved enzyme, which is believed to cleave large dsRNA to produce siRNA *in vivo,* has been identified as Dicer (Bernstein, et al., *Nature* 409:363-366 (2001)). This enzyme contains a helicase motif, a PAZ (PIWI-ARGONAUT-ZWILLE) domain and a tandem repeat of a catalytic domain, which is RNaseIII-like. Drosophila extracts presumably containing Dicer mixed with large dsRNA *in vitro* produce short dsRNA in a range of sizes. The preferred size for RNAi applications in this mixture was determined by Tuschl et al. to be 21-23 nucleotides (International Publication No. WO 01/75164). Problems associated with using crude cell extracts containing a putative cleavage enzyme are, for example, that it is unclear what proteins in the mixture of proteins are necessary and sufficient to generate the observed effect. In addition, the extract is relatively inefficient at cleaving large dsRNA with only a relatively small amount of the starting material being cleaved to the desired size *in vitro* even under extended incubation times. (Paddison et al., *Proc. Natl. Acad. Sci.* 99:1443-1448 (2002)).